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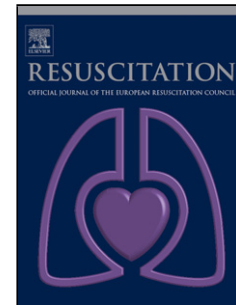
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Spatiotemporal AED optimization is generalizable

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Abstract:

Aims: Mathematical optimization of automated external defibrillator (AED) placements has the potential to improve out-of-hospital cardiac arrest (OHCA) coverage and reverse the negative effects of limited AED accessibility. However, the generalizability of optimization approaches has not yet been investigated. Our goal is to examine the performance and generalizability of a spatiotemporal AED placement optimization methodology, initially developed for Toronto, Canada, to the new study setting of Copenhagen, Denmark.

Methods: We identified all public OHCA (1994-2016) and all registered AEDs (2016) in Copenhagen, Denmark. We calculated the coverage loss associated with limited temporal accessibility of registered AEDs, and used a spatiotemporal optimization model to quantify the potential coverage gain of optimized AED deployment. Coverage gain of spatiotemporal deployment over a spatial-only solution was quantified through 10-fold cross-validation. Statistical testing was performed using χ^2 and McNemar's tests.

Results: We found 2,149 public OHCA and 1,573 registered AED locations. Coverage loss was found to be 24.4% (1,104 OHCA covered under assumed 24/7 coverage, and 835 OHCA under actual coverage). The coverage gain from using the spatiotemporal model over a spatial-only approach was 15.3%. Temporal and geographical trends in coverage gain were similar to Toronto.

Conclusions: Without modification, a previously developed spatiotemporal AED optimization approach was applied to Copenhagen, resulting in similar OHCA coverage findings as Toronto, despite large geographic and cultural differences between the two cities. In addition to reinforcing the importance of temporal accessibility of AEDs, these similarities demonstrate the generalizability of optimization approaches to improve AED placement and accessibility.

Keywords: Resuscitation; cardiac arrest; public access defibrillation; automated external defibrillator

Introduction:

Out-of-hospital cardiac arrest (OHCA) affects over 700,000 people a year in North America and Europe[1, 2]. Survival from OHCA decreases rapidly for every minute delay in treatment[3]. Treatment options include cardiopulmonary resuscitation (CPR) and defibrillation. In particular, publicly located automated external defibrillators (AEDs) can be used by bystanders to reduce the delay to defibrillation for OHCA victims[3-6]. Consequently, much effort has focused on implementing public access defibrillator (PAD) programs and developing guidelines for strategic AED placement, which recommend AEDs be placed in high-risk areas and be easily reachable within a few minutes[7, 8]. Prior research has focused on quantifying OHCA risk in different location types in cities worldwide, demonstrating generalizability of many of the findings[3, 6, 9-14]. For example, transportation and recreation facilities have been established in multiple studies as high-risk areas that can benefit from AED placement[3, 6, 9, 15]. In practice, AEDs may be positioned based on local or political decisions, resulting in paradoxical placement in low risk areas[9, 16].

For an AED to be used it needs to be accessible. Previous research has shown that in North America and Europe, inaccessible AEDs can significantly decrease OHCA coverage[17], in particular by over 50% during the weekends, evening, and night times[18]. To better guide AED placement and temporal AED accessibility, current research has focused on mathematical optimization of AED placements[17, 19-23]. Studies from Toronto, Canada, suggest that optimizing AED locations can outperform population-guided strategies[19], reverse the negative effects of limited temporal availability[17], and be cost-effective[22]. However, unlike the

findings on OHCA risk in different location types, it is currently unclear whether the optimization methodologies and results are generalizable. Establishing generalizability is particularly important since the potential financial benefits of optimization strategies can be realized through more efficient PAD programs, many of which have low utilization despite widespread and costly AED deployment[24].

The current paper presents the first study to determine generalizability of previous optimization research for AED placement. In particular, we use the methodology from the spatiotemporal optimization study from Toronto, Canada[17], and apply it to a new study setting of Copenhagen, Denmark. We perform two analyses using Copenhagen data: 1) quantify the temporal availabilities and OHCA coverage of existing registered AEDs, and 2) measure the improvement in AED accessibility and OHCA coverage from spatiotemporal optimization of AED locations. Copenhagen and Toronto are contrasting in size, population, city structure, existing AED networks, and working hours[9, 17, 25-31]. Given these differences, establishing generalizability to Copenhagen suggests that optimization will be effective in other settings as well.

Methods:

Study Setting

Central Copenhagen has a population of roughly 600,000 and spans approximately 97 square km[30]. The Copenhagen Emergency Medical Service (EMS) system is a two-tiered system, which consists of ambulances staffed by paramedics providing basic life support, and mobile emergency care units (MECUs) staffed by physicians providing advanced life support. Both EMS tiers are deployed simultaneously by the Emergency Medical Dispatch Centers (EMDCs) during a cardiac arrest.

Study design and data sources

This was a retrospective, registry-based study using data on OHCA documented by the Copenhagen MECUs physicians. The study population included all public location OHCA of presumed cardiac cause in the city of Copenhagen, Denmark, from 1994-2016. Data abstraction on the historical OHCA included the Utstein predictors of outcome, specifically demographic characteristics, circumstances of arrest and characteristics of care, and the primary outcome of survival. Information regarding bystander witnessed collapse, bystander CPR, and bystander defibrillation before EMS arrival was available during 2008-2016. Public locations were defined as areas accessible to the general public and included outdoor locations, public transportation sites, schools, outpatient clinics, commercial and civic buildings, and exclude hospitals.

All publicly available AEDs registered with the Danish AED Network (<https://hjertestarter.dk/>) by the end of 2016 in central Copenhagen were included. The registry is managed by a private foundation and contains detailed information on AED location, temporal availability and date of registration. The AEDs in this registry are linked directly with Copenhagen EMS to allow dispatchers to identify the closest available AEDs for lay responders to obtain and use in the case of an OHCA. AED registration information is confirmed by network staff members prior to including the AED location in the registry[25]. By the end of 2016, there were 1,573 registered publicly available AEDs in central Copenhagen (262.2 AEDs per 100,000 inhabitants).

A dataset of candidate locations to examine for potential AED placement in Copenhagen, composed of 2,138 businesses and public points of interest, was collected from January – March 2017. Candidate locations were selected based on common and popular buildings because of our focus on public OHCA and were equivalent counterparts to locations selected in Toronto,

Canada.[17] The exact location and hours of operations was collected by Viamap®, a private cooperation, as well as through online resources and data extraction from websites.

Analysis 1: Temporal availability and coverage loss of registered AEDs

We calculated OHCA coverage based on two definitions. First, we calculated *assumed 24/7 coverage*, where an OHCA was considered covered if it occurred within 100 m of an AED. Second, we calculated *actual coverage*, where an OHCA was considered covered if it occurred within 100 m of an AED and when the AED was available at the time of the OHCA. Locations housing an AED were defined as temporally inaccessible when they are closed according to their hours of operation. The 100 m coverage radius was selected as an approximation of the maximum round trip distance a bystander could travel to retrieve and setup an AED within 3 minutes[7, 8, 19].

Using the coverage definitions, we then calculated *coverage loss*, which was defined as *assumed 24/7 coverage* minus *actual coverage*, and then divided by *assumed 24/7 coverage*. *Coverage loss* was examined for different times of day (daytime, 8:00 AM – 3:59 PM; evening, 4:00 PM – 11:59 PM; night, 12:00 AM – 7:59 AM), days of the week (weekday and weekend), geographic areas (city center and outside city center), and by location types where the registered AEDs were placed. The 95% confidence intervals (CI) were calculated for the *coverage loss* using an error propagation and paired proportions approach to change absolute to *coverage loss* CIs. To test for statistical significance in coverage loss across the disjoint and unpaired categories (time of day, day of week, and geography), a chi-squared test was used, where a 2-tailed value of $P < 0.05$ was considered significant.

Analysis 2: Spatiotemporal optimization of AED placements

We used a previously developed spatiotemporal optimization model[17], which accounts for both spatial and temporal information of OHCA events and candidate AED locations, to choose the optimal locations to place AEDs and maximize OHCA coverage based on historical OHCA incidence. The model, applied to the Copenhagen data, was unmodified from its initial development in Toronto. The spatiotemporal model used the following inputs: 1) addresses and hours of operation of existing registered AED locations, 2) locations and times of historical OHCA, 3) addresses and hours of operation of candidate AED locations, and 4) a user-specified model parameter N , which determines the number of candidate locations where AEDs are to be placed. The model outputted the N selected locations that together maximized *actual coverage* of historical OHCA, along with the total number of OHCA covered.

The spatiotemporal optimization model was compared to a spatial-only optimization model[19], which works similarly to the spatiotemporal model, but does not consider the time of the OHCA and the hours of operation of the candidate AED locations. The two models were evaluated on the improvement in *actual coverage* on top of the baseline coverage provided by existing registered AEDs (model input #1) of historical OHCA in Copenhagen. To ensure the comparison of the two models is based on out-of-sample data, we used a 10-fold cross validation approach in which the OHCA not covered by the existing registered AEDs were divided randomly into 10 disjoint sets of approximately equal size. In each fold, one set was used as a testing set, while the remaining nine sets were used as the training set. The testing sets across each fold were disjoint.

For each fold, the optimization models used the training sets as the historical OHCA data (model input #2) to select the optimal AED locations from the candidate AED locations (model input #3). The optimal locations determined by the spatiotemporal and spatial-only models were

then evaluated on *actual coverage* using that fold's testing set. This process was carried out for all 10 folds, producing *actual coverage* values for each of the 10 testing sets. The results reported in this study represent the totals over the 10 folds. The models were run for values of N (model input #4), ranging from 50 to 200 in increments of 50 for each fold (i.e. $N = 50, 100, 150, 200$).

The *coverage gain* was calculated for each N and was defined as the *actual coverage* from the spatiotemporal model minus *actual coverage* from the spatial-only model, and then divided all by *actual coverage* from the spatial-only model. *Overall coverage gain* was calculated by taking the weighted mean of the *coverage gain* for each N , weighted by the *actual coverage* values from the spatial-only model. The 95% CIs were computed for the *overall coverage gain*, as well as for the *coverage gain* broken down by time of day, day of week, and geography. The difference in *actual coverage* between the two models was determined to be significant using McNemar's test for each N , where a 2-tailed value of $P < 0.05$ was considered significant.

Results:

There were 2,149 public OHCA of presumed cardiac cause in Copenhagen, Denmark between 1994 – 2016 (Table 1). A total of 653 public non EMS-witnessed OHCA occurred between 2008 – 2016 where bystander response information was readily available. There was no significant difference in rates between pre-specified time of day intervals for received bystander CPR ($P = 0.37$), received bystander defibrillation ($P = 0.79$) arrests, and 30-day survival ($P = 0.06$). Bystander-witnessed rates were significantly associated with different time intervals ($P = 0.002$).

Public OHCA incidence (1994-2016) by time of day, day of week, and geography is shown in Online Table 1. Online Table 2 shows a similar categorization for arrests that received

bystander defibrillation (2008 – 2016). The majority of registered AEDs, 1,243 of 1,573 (79.0%), were not available 24/7, and 997 (63.4%) were unavailable on weekends. The availabilities of these AEDs by time interval and day of week as compared to previously published Toronto AED availabilities[17] are shown in Fig. 1 (A;B). AEDs availabilities are much greater during the weekdays compared to weekends in Copenhagen.

Analysis 1: Temporal availability and coverage loss of registered AEDs

The registered AEDs covered 1,104 OHCA (51.3%) under *assumed 24/7 coverage* and 835 (38.9%) under *actual coverage*, corresponding to a *coverage loss* of 24.4% of the 2,149 public OHCA included in the study. The coverage losses by time of day and geography, compared across cities are shown in Table 2. Overall coverage loss during the daytime, evening, and night was significant ($P < 0.001$). The differences in coverage loss across time of days was also significant for Weekdays ($P < 0.001$), City Center ($P < 0.001$), and Outside City Center ($P < 0.001$) splits, but not for weekends ($P = 0.284$). Overall coverage loss during the weekend and weekday ($P < 0.001$) as well as city center and outside city center ($P < 0.05$), were both significantly different. City center and outside city center definitions are equivalent to Toronto's downtown and not downtown categories in Table 2. The majority of all OHCA occurred during the weekends, evenings, and night and experienced a coverage loss of 38%.

Coverage loss due to AED inaccessibility during the weekend in the city center (36.7%) and outside city center (43.6%) was more than double that of the weekday city center (15.0%) and outside city center counterparts (20.2%) and all differences were significant ($P < 0.001$) (Online Table 3).

The coverage loss categorized by AED location type is shown in Online Table 4. Companies and office buildings accounted for the most registered AEDs as well as providing

access for most of the OHCAs covered under both *assumed 24/7 coverage* and *actual coverage*. Four of the top five location types with the most registered AEDs, accounted for 62.8% of all deployed AEDs, and had a coverage loss exceeding 40% based on actual coverage. Coverage loss was minimal for both transportation facilities (0.9%) and residential settings (4.7%).

Analysis 2: Spatiotemporal optimization of AED placements

The 835 OHCAs covered by the registered AEDs were excluded from the analysis; the remaining 1,314 OHCAs were used in the 10-fold cross validation analysis.

Fig. 2 shows the *coverage gain* from the AED placements selected by the spatiotemporal over the spatial-only model split by time of day, day of week and geography. The *overall coverage gain* was 15.3% (95% CI: 12.7% – 17.9%). The coverage gain in AED accessibility was statistically significant for all categories ($P < 0.05$) except for Copenhagen – City Center. The difference in *actual coverage* values were statistically significant ($P < 0.005$) for all N (Fig. 3). Additional placement of AEDs above $N = 200$ does not provide an increase in coverage because all of the historical OHCAs that are within range of the candidate locations are covered by this point. The coverage values for each N for each OHCA category split are shown in the Appendix (Online Fig. 1-7). The 15.3% coverage gain was determined to be equivalent to a 21.2% gain in efficiency of AED placements. That is, when using the spatiotemporal model to optimize AED placements, 21.2% fewer AEDs are required to reach the same level of coverage as the spatial-only model (Online Table 5).

Discussion:

This study offers support for the generalizability of mathematical optimization approaches for AED placement. Similar to findings from a previous study in Toronto[17], a spatiotemporal optimization model was able to identify AED placements in Copenhagen that

could reverse the coverage loss associated with limited temporal availabilities of existing AEDs. In Toronto, a coverage loss of 21.5% was observed, which could be offset by a coverage gain of 25.3% through spatiotemporal optimization. In comparison, a coverage loss of 24.4% was observed in Copenhagen, while spatiotemporal optimization generated a coverage gain of 15.3%. Despite significant differences between the cities, including Copenhagen's smaller total population[27, 30, 31], higher population density[27, 30, 31], city structure[28, 31], demographic consisting of fewer individuals of differing ethnic origins[30-32], larger AED network size[17], and shorter working hours[26, 29], the similar coverage loss/gain trends reinforce the finding that temporal accessibility is a critical and potentially widespread issue that should be considered for AED placement guidelines and that may be addressed through spatiotemporal optimization.

Although the OHCA coverage gains in Copenhagen followed the same trend seen in Toronto, the magnitude of the gains was lower. One factor could be that our model optimizes placements on top of the already existing registered AED network. If an AED network is already well-designed and provides high OHCA coverage, there is less opportunity for the spatiotemporal model to increase coverage. For example, the number of AEDs deployed in Copenhagen has increased 15-fold from 6 to 92 AEDs/100,000 inhabitants from 2007-2011[25] and is at 262.2 AEDs/100,000 inhabitants as of 2016, reducing coverage loss due to limited temporal availability from 33.5% in 2011 to 24.4% in 2016[18]. Limited temporal availabilities of candidate AED locations might also reduce the coverage gain. For example, 62.1% of Copenhagen buildings containing AEDs were closed on weekend, compared to 28.6% in Toronto. Furthermore, there was generally more consistency in opening hours of candidate locations in Copenhagen. As a result, optimization for spatial coverage would be similar to

optimization for spatiotemporal coverage, resulting in less of an advantage for the spatiotemporal optimization model.

Nevertheless, a 15.3% coverage gain represents a significant opportunity for improvement given the high coverage loss overall in Copenhagen. Copenhagen, due to its high bystander intervention rate, which is fairly stable across all times of day, may be better positioned to realize the benefits of improved AED accessibility associated with the coverage gain. In general, a combination of a willing bystander population, strong dispatch-assisted bystander support, and strategies to help retrieve nearby AEDs are needed to capture the coverage gains projected through spatiotemporal optimization.

Significant costs and inefficient use of resources is a critical issue confronting many PAD programs[16, 24, 33]. Studies have noted that the cost-effectiveness of PAD programs hinge on the frequency of AED use[34, 35]. Optimization may be able to improve cost-effectiveness of PAD programs by identifying optimal locations to place AEDs. Equivalently, as our efficiency analysis suggests, optimization can help PAD programs achieve comparable coverage levels with fewer resources.

Although the spatiotemporal optimization approach is general, applying it to other cities may require a varying level of effort depending on data availability and completeness, including historical OHCA data, locations and availabilities of existing AEDs, and candidate locations for AEDs. We also note that even with detailed data regarding OHCA and AEDs, there may be additional factors, such as registered AEDs with expired batteries or pads, that impact the true availability of AEDs.

Improving AED placement through optimization is only one of the many ways to contribute towards improving bystander defibrillation and OHCA survival. Increasing the rate of

bystander intervention, reducing the delay to bystander response[36], or improving access to AEDs either through placements that facilitate 24/7 availability or innovations that deliver an AED to the patient side[21] are all important factors that may substantially increase the chances of early defibrillation and ultimately survival.

Conclusion:

Optimization of AED placements is a promising approach to support PAD program development, improve OHCA coverage and AED usage, and improve utilization of scarce and costly resources. This study is the first to validate the potential gains due to optimization in a new study setting (Copenhagen) from the one in which the model was initially developed (Toronto). This finding suggests that the benefits of optimizing AED placements can be generalized to new settings to improve OHCA response and PAD programs worldwide.

Conflicts of Interest:

None.

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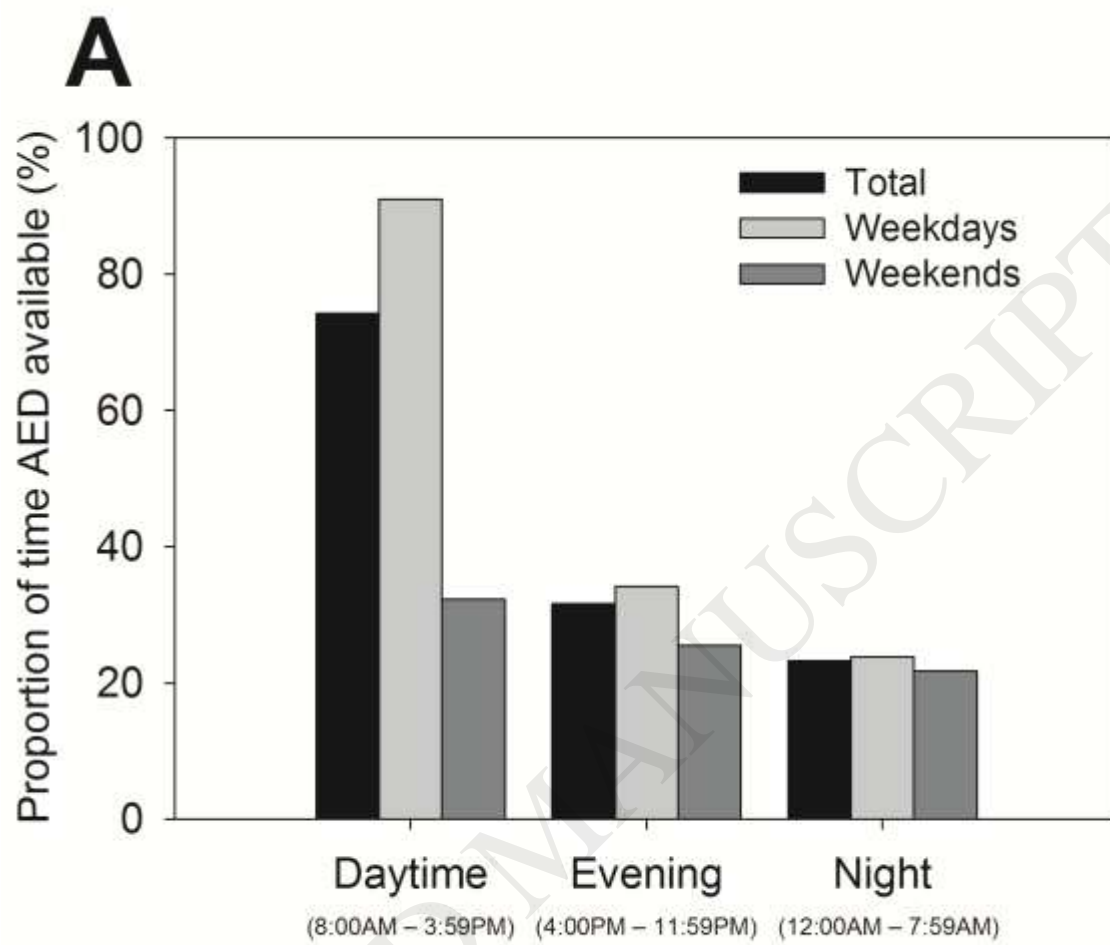
[36] Ringh M, Rosenqvist M, Hollenberg J, Jonsson M, Fredman D, Nordberg P, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. *N Engl J Med*. 2015;372:2316-25.

Legends to Figures:

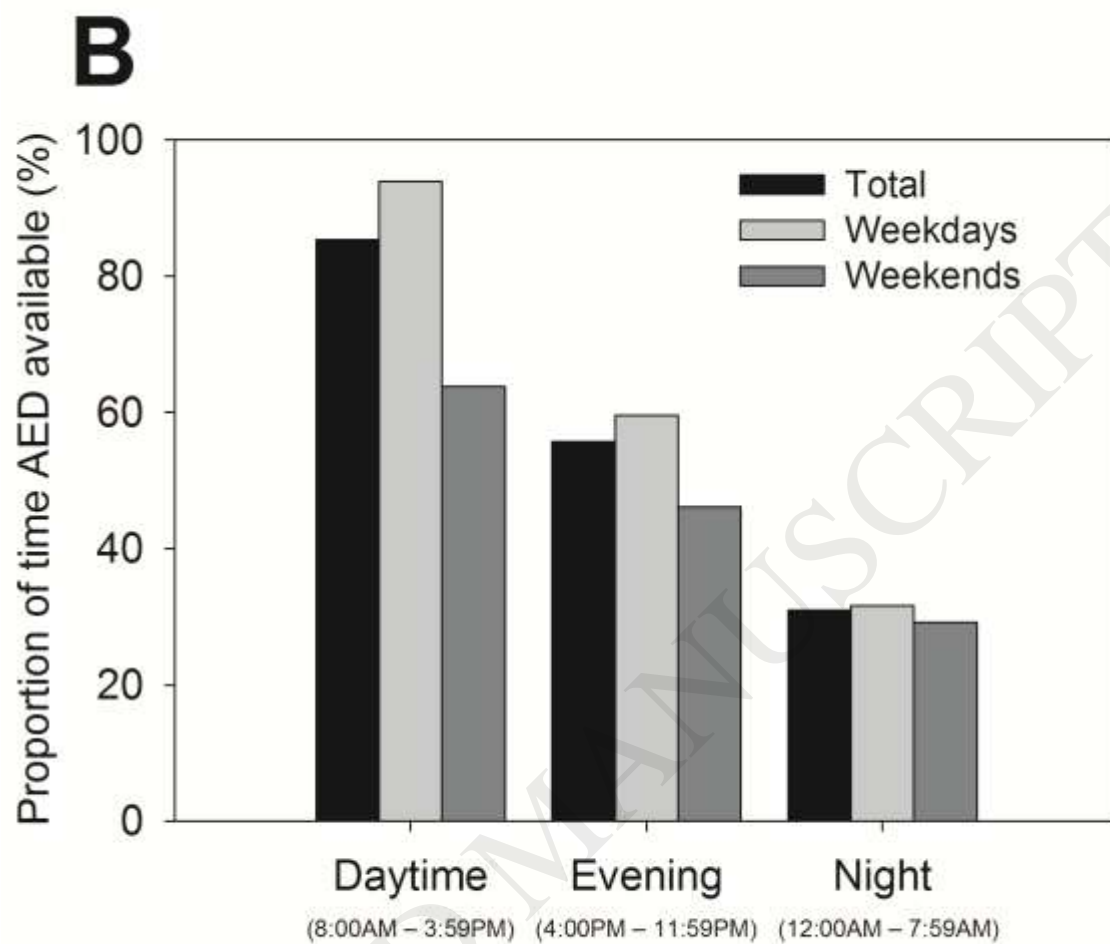
Figure 1. Accessibility of registered AEDs. AED accessibility by time of day, day of week and geography. AED accessibility over times of day for A: Copenhagen (N=1,573), B: Toronto (N=737). Figure 1 B: Reprinted from The Journal of the American College of Cardiology, Vol. 68 No. 8, Sun CLF, Demirtas D, Brooks SC, Morrison LJ, Chan TCY, Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization, Pages 836-45, 2016, with permission from Elsevier.

Figure 2. OHCA coverage gain using the spatiotemporal model. AED accessibility for OHCA as defined as coverage gains in *actual coverage* of the testing set OHCA when using the spatiotemporal model over the spatial-only model. The coverage gains were calculated as the weighted mean of the coverage gain for each N , weighted by the *actual coverage* values of the spatial-only model. Toronto data in Figure 2: Reprinted from The Journal of the American College of Cardiology, Vol. 68 No. 8, Sun CLF, Demirtas D, Brooks SC, Morrison LJ, Chan TCY, Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization, Pages 836-45, 2016, with permission from Elsevier.

Figure 3. Comparing Actual AED accessibility for OHCA based on coverage values of the spatiotemporal and spatial-only model in Copenhagen. The *actual coverage* of testing set OHCA from registered AED locations selected by the spatiotemporal and spatial-only models.

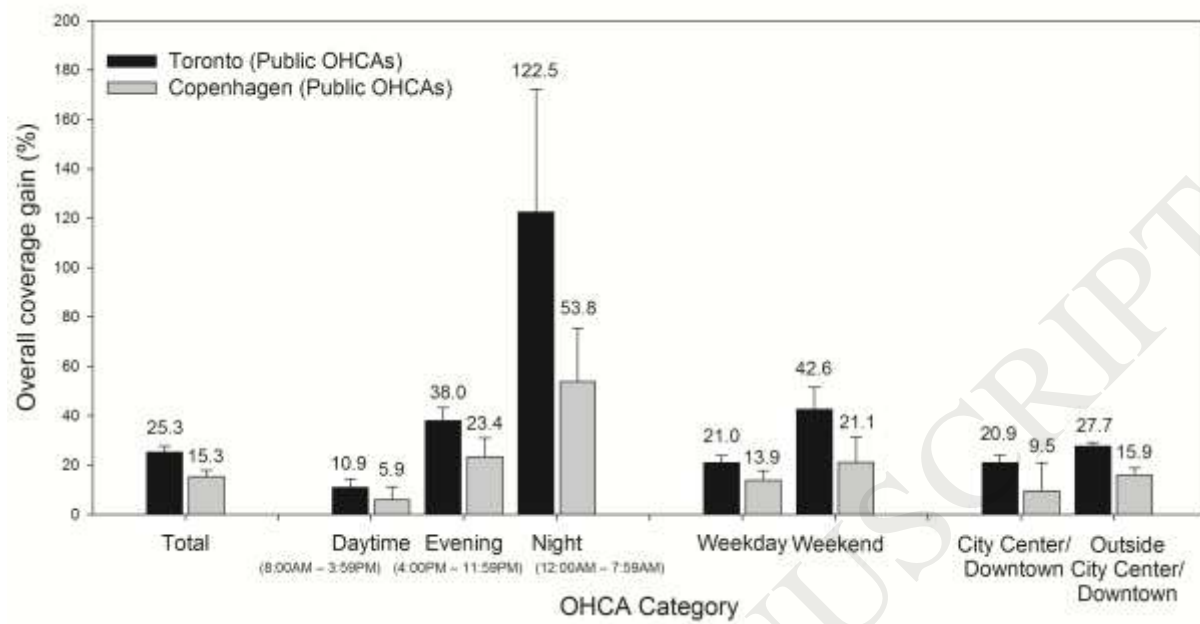


Figr-1



Figr-2

Fig-3



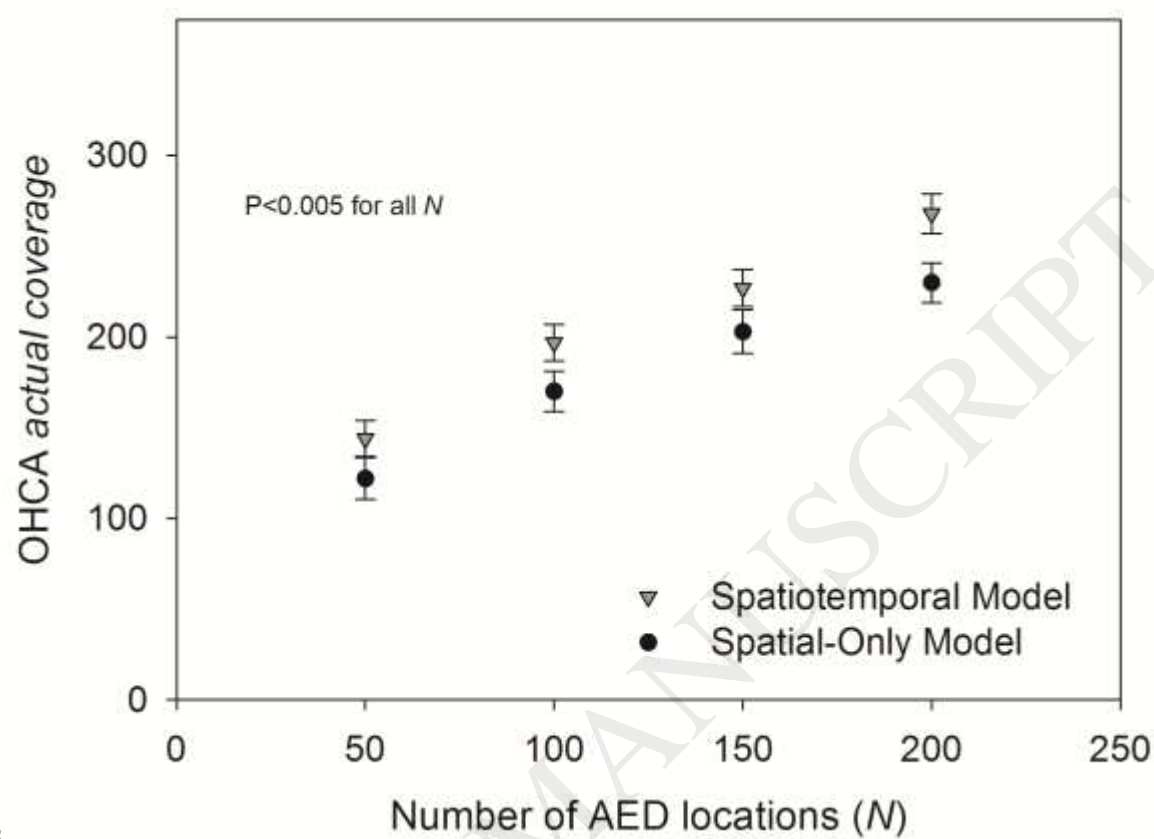


Fig-3

Table 1. Baseline Characteristics of Public OHCA in Copenhagen

OHCA from 1994 to 2016[*]	Total (n=2,149)	Daytime (8:00AM - 3:59PM) (n=1,148)	Evening (4:00PM -11:59PM) (n=714)	Night (12:00AM - 7:59AM) (n=287)
Median age, y (IQR)	63 (51-75)	66 (54-77)	62 (49-74)	55 (44-69)
Men	61 (50-72)	62 (52-74)	61 (48-70)	54 (43-66)
Women	74 (59-82)	76 (65-83)	72 (55-81)	67 (47-81)
Male sex, n (%)	1,608 (75.6)	844 (74.8)	539 (75.5)	225 (79.2)
Median response time, min (IQR)[†]	5 (3-6)	5 (3-6)	5 (3-6)	5 (4-7)
Shockable initial heart rhythm, n (%)	829 (38.6)	492 (42.9)	268 (37.5)	69 (24.0)
OHCA from 2008-2016[‡]	Total (n=653)	Daytime (8:00AM - 3:59PM) (n=354)	Evening (4:00PM -11:59PM) (n=201)	Night (12:00AM - 7:59AM) (n=98)
Bystander-witnessed arrest, n (%)	438 (69.9)	255 (76.6)	131 (66.5)	52 (53.6)
Received bystander CPR, n (%)	440 (70.4)	242 (72.7)	138 (70.4)	60 (62.5)
Received bystander defibrillation, n (%)	94 (14.6)	53 (15.2)	29 (14.5)	12 (12.5)
30-day survival, n (%)	218 (35.2)	125 (37.0)	71 (36.8)	22 (24.7)

^{*}Number of missing for variables available and described from 1994-2016: age (n=45), sex (n=22), and response time (n=16). A total of 2,087 of 2,149 OHCA were complete for all variables.

[†]Time interval from the dispatch of the EMS to vehicle arrival at scene[†].

[‡]The following variables were only available for cardiac arrests from 2008 through 2016 and includes only known non EMS-witnessed arrests: n=71 OHCA excluded due to EMS-witnessed arrests; n=4 OHCA excluded due to missing information on EMS-witnessed status. Number of missing: bystander-witnessed arrest (n=26), bystander CPR (n=28), bystander defibrillation (n=8).

30-day survival: n=33 OHCA's excluded due to invalid personal identification number. A total of 587 of 653 OHCA's were complete for all variables.

EMS=emergency medical service; CPR=cardiopulmonary resuscitation; OHCA=out-of-hospital cardiac arrest.

Table 2. Summary of OHCA coverage loss of registered AEDs. Right side (Toronto) of Table 2: Reprinted from The Journal of the American College of Cardiology, Vol. 68 No. 8, Sun CLF, Demirtas D, Brooks SC, Morrison LJ, Chan TCY, Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization, Pages 836-45, 2016, with permission from Elsevier.

Copenhagen						Toronto						
Total	Assumed 24/7 coverage	Daytime				Total	Daytime					
		Evening (8:00A - 3:59PM)	Night (12:00A - 7:59AM)	Evening (4:00PM - 11:59PM)	Night (12:00A - 7:59AM)		Evening (4:00PM - 11:59PM)	Night (12:00A - 7:59AM)				
(n=2149)	(n=1148)	(n=714)	(n=287)	(n=2440)	(n=1252)	(n=840)	(n=348)					
Total	Assumed 24/7 coverage	1104	575	377	152	451	221	168	62	Total		
		Actual coverage	835	510	242	83	354	202	120		32	(n=2440)
Coverage loss (%)	24.4	11.3	35.8	45.4	21.5	8.6	28.6	48.4				
Weekday	Assumed 24/7 coverage	840	442	301	97	342	176	122	44	Weekdays		
		Actual coverage	682	428	198	56	279	166	90		23	(n=1778)

	Coverage loss (%)	18.8	3.2	34.2	42.3	18.4	5.7	26.2	47.7	
Weekend	<i>Assumed 24/7 coverage</i>	264	133	76	55	109	45	46	18	Weekends
(n=539)	<i>Actual coverage</i>	153	82	44	27	75	36	30	9	(n=662)
	Coverage loss (%)	42.0	38.3	42.1	50.9	31.2	20.0	34.8	50.0	
City Center	<i>Assumed 24/7 coverage</i>	280	151	88	41	158	74	59	25	Downtown
(n=349)	<i>Actual coverage</i>	225	141	59	25	130	67	47	16	(n=469)
	Coverage loss (%)	19.6	6.6	33.0	39.0	17.7	9.5	20.3	36.0	
Outside City Center	<i>Assumed 24/7 coverage</i>	824	424	289	111	293	147	109	37	Outside
(n=1800)	<i>Actual coverage</i>	610	369	183	58	224	135	73	16	Downtown
	Coverage loss (%)	26.0	13.0	36.7	47.7	23.6	8.2	33.0	56.8	(n=1971)

ACCEPTED MANUSCRIPT